Place in the file history of the subject Application a marked-up version of Page 1 (attached hereto) showing a new Title and showing status of parent applications.

USE OF PROPARGYL GLYCINE AMINO PROPARGYL DIOL COMPOUNDS FOR TREATMENT OF [HYPERTENSION] RENAL FAILURE

RELATED APPLICATIONS

[This application is a continuation-in-part of Application Serial No. 07/784,272, filed on 29 October 1991.] This application is a divisional of U.S. Application Serial No. 09/479,280, filed 6 January 2000, which issued as U.S. Patent No. 6,342,624, which is a continuation of Application Serial No. 09/969,522 filed on 13 November 1997, which is a continuation of Application Serial No. 08/771,334, filed on 16 January 1996, which is a continuation of Application Serial No. 08/199,237, filed 28 February 1994, which issued 16 January 1996 as U.S. Patent 5,484,812, which is a continuation-in-part of Application Serial No. 07/784,272, filed on 29 October 1991, which issued on 29 June 1993 as U.S. Patent No. 5,223,535.

FIELD OF THE INVENTION

Renin-inhibiting compounds are known for control of hypertension. Of particular interest herein are compounds useful as renin inhibiting agents.

BACKGROUND OF THE INVENTION

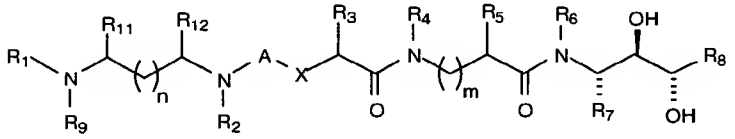
Renin is a proteolytic enzyme produced and secreted into the bloodstream by the juxtaglomerular cells of the kidney. In the bloodstream, renin cleaves a peptide bond in the serum protein angiotensinogen to produce a decapeptide known as angiotensin I. A second enzyme known as angiotensin converting enzyme, cleaves angiotensin I to produce the octapeptide known as angiotensin II. Angiotensin II is a potent pressor agent responsible for vasoconstriction and elevation of cardiovascular pressure. Attempts have been made to control hypertension by blocking the action of renin or by blocking the formation of angiotensin II in the body with inhibitors of angiotensin I converting enzyme.

Classes of compounds published as inhibitors of the action of renin on angiotensinogen include renin antibodies, pepstatin and its analogs, phospholipids, angiotensinogen analogs, pro-renin related analogs and peptide aldehydes.

USE OF PROPARGYL GLYCINE AMINO PROPARGYL DIOL COMPOUNDS FOR TREATMENT OF [HYPERTENSION] RENAL FAILURE

ABSTRACT

Compounds characterized generally as propargyl glycine amino propargyl diol derivatives are useful for treatment of [hypertension] renal failure. Compounds of particular interest are those of Formula I



(I)

wherein A is selected from CO and SO_2 wherein X is selected from oxygen atom and methylene; wherein each of R_1 and R_9 is a group independently selected from hydrido, methyl, ethyl, n-propyl, isopropyl, benzyl, b, b, b-trifluoroethyl, t-butyloxycarbonyl and methoxymethylcarbonyl, and wherein the nitrogen atom to which R_1 and R_9 are attached may be combined with oxygen to form an N-oxide; wherein R_2 is selected from hydrido, methyl, ethyl and isopropyl; wherein R_3 is selected from benzyl, cyclohexylmethyl, phenethyl, imidazolemethyl, pyridylmethyl and 2-pyridylethyl; wherein each of R_5 and R_8 is independently propargyl or a propargyl-containing moiety; wherein R_7 is cyclohexylmethyl; wherein each of R_4 and R_6 is independently selected from hydrido and methyl; wherein each of R_{11} and R_{12} is independently selected from hydrido, alkyl and phenyl; wherein m is zero; and wherein n is a number selected from zero through three; or a pharmaceutically-acceptable salt thereof.